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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/662,640	09/15/2003	Andrea Liebmann-Vinson	P-5803	9402

64154 7590 07/18/2007

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EXAMINER	
AGRAWAL, RITESH	
ART UNIT	**PAPER NUMBER**
1631	

MAIL DATE	DELIVERY MODE
07/18/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/662,640	LIEBMANN-VINSON ET AL.	
	Examiner	Art Unit	
	Ritesh Agrawal	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 February 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,5-7,11-14 and 17-19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3, 5-7, 11-14, and 17-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicants' amendment and request for reconsideration in the communication filed on 2/28/07 are acknowledged and the amendments entered.

Claims 1-3, 5-7, 11-14, and 17-19 are currently pending and under consideration.

Withdrawn Rejections

2. The rejection of claims 1-3, 5-7, 11-14, and 16-19 under 35 U.S.C. 112, first paragraph, a scope enablement rejection, is withdrawn in light of the amendments to the claims filed 2/28/07.

The rejection of claims 1-3, 5-7, and 19 under 35 U.S.C. 102(b) over Eggers is withdrawn in light of applicants' amendments filed 2/28/07.

The provisional rejection of claims 1-3, 5, 7, and 17-18 as being obvious over claims of application number 10/662,713 is withdrawn in light of applicants' amendments filed 2/28/07.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

3. Claims 1-3, 5-7, and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Eggers, US 5,532,128, in view of *A* Field Guide to Experimental Design, August 16,2000, at http://www.tfrec.wsu.edu/ANOVA/Latin.html, retrieved 5/30/2006. This rejection is modified from the previous Office action, but the modification was necessitated by amendment.

With respect to claims 1, 2, and 19, Eggers discloses a method for identifying a molecule within a sample substance (abstract). Eggers discloses receptacles having a culture surface (e.g., fig. 6-7; col. 7, line 60 through col. 8, line 67). Eggers discloses

placing different mixtures of agents (probes, *e.g.,* oligos, proteins, antibodies, antigens) into the receptacles (fig. 2,6-7; claims 2-10; col. 5, lines 16-43; col. 7, lines 61 -66; col. 10, lines 44-59) according to a statistical design (col. 5, tables I-II). Eggers discloses immobilizing a mixture of probes to a culture surface (fig. 2, 6-7; col. 7, line 60 through col. 8, line 67). Eggers discloses contacting agents with whole cells (fig. 7; col. 4, lines 3-8; col. 1 1, lines1 1-30; claim 5). Eggers discloses acquiring data indicative of a desired biological response (e.g., binding to an antibody, oligo, protein) (fig. 1, 5; col. 1-2 discussing optical, fluorescent, radioactive detection methods; claim 1). Eggers discloses identifying agents producing desired binding (biological response) using statistical modeling of acquired data (col. 6, line 1 through col. 7, line 30).

However, Eggers does not specifically teach a Latin square design as in amended claim 1.

A Field Guide teaches using the Latin square design for controlling the variation in an experiment that is related to rows and columns.

With respect to claim 3, Eggers discloses a culture surface coated with an agent-immobilized material (col. 7, lines 60 through col. 8, lines 67) 3.

With respect to claim 5, Eggers discloses an agent-immobilized material containing reactive groups for covalently immobilizing agents (col. 7, lines 60 through col. 8, lines 67).

With respect to claim 6, Eggers discloses agent-immobilizing material on a culture surface that does not support adhesion (col. 7-8, section Probes).

With respect to claim 7, Eggers discloses cell adhesion ligand-agents (fig. 7, col. 11, lines 10-35).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to modify the method of Eggers to use a Latin square design, such as taught by A Field Guide, where the motivation would have been to control variations in two different directions, as taught by A Field Guide.

Applicants' arguments have been fully considered, but they are not found persuasive.

Applicants argue that there is no motivation to combine the teachings of Eggers and the A field Guide reference because the references are in different fields of endeavor (remarks, page 7, last paragraph through page 8, 1st paragraph).

In response, it is noted that the present invention falls within the field of bioinformatics. One of ordinary skill in the art of bioinformatics would be knowledgeable in both the biological teachings of Eggers and the statistical teachings of the Field Guide reference. Bioinformaticians are constantly applying established statistical methods to biological problems to increase the speed and accuracy of biological discovery. Given the teachings of the Field Guide reference and the use of an array type structure by Eggers (comprising columns and rows) one of ordinary skill in the art of bioinformatics would clearly be motivated to combine the reference teachings.

4. Claims 1-3, 5-7, 11, and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cima, US 5,906,828, in view of Falsey, Bioconjugate Chem., 12:346-

353 (2001), and further in view of Greco, Pharmacological *Rev.*, 47(2):33 1-385 (1995) and further in view of *A* Field Guide to Experimental Design, August 16,2000, at http://www.tfrec.wsu.edu/ANOVA/Latin.html, retrieved 5/30/2006. This rejection is modified from the previous Office action, but the modification was necessitated by amendment.

Cima discloses a method a method for screening compounds for effects on cell growth, proliferation, metabolism, and DNA synthesis (col. 10, lines 50-58). Cima discloses immobilizing mixtures of agents on a solid support (col. 2, line 55 through col. 3,line5; col. 6, lines 24-38; col. 7, lines 37-45; col. 7, lines 8-35; col. 8, line 66 through col. 9, line 3; claim 1). Cima discloses growth effector molecules as being immobilized agents (col. 6, lines 24-38). Cima discloses contacting mixtures of agents with a whole cell (col. 13, lines 38-56; claim 1). Cima discloses acquiring desired biological response and identifying mixtures of agents having effect in producing a desired biological effect (col. 3, lines 2-5; col. 6, lines 24-38; col. 9, lines 12-17; col. 10, lines 50-58; example 1). Cima discloses using a statistical design for obtaining different mixtures of agents (col. 7, lines 37-48). Cima discloses coating with an agent immobilized material wherein the material may contain groups for covalent immobilization of an agent (col. 5-6, section Attachment Substrates and col. 7, Attachment Methods). Cima discloses optionally using a coating which enhances the attachment of cells to a surface (col. 6, lines 16-22).

Although Cima discloses using a membrane and a 96-well manifold apparatus for dotblot assay, Cima does not specifically disclose using receptacles for placing agent

mixtures. Cima does not disclose using statistical models for identifying a mixture. Cima also does not disclose the use of a Latin Square Design.

Falsey discloses using a peptide and small molecule arrays for high throughput cell adhesion and functional assays (abstract). Falsey discloses using a 96 well plate for microarray spotting (p. 347, right col.).

Greco discloses using a statistical design (p. 373-376) and statistical models (fig. 1, text on p. 334-335) for assessing synergistic effect (i.e., biological response) of mixtures of agents (see, for example, p. 376, right col. and table 3 on p. 350).

A Field Guide teaches using the Latin square design for controlling the variation in an experiment that is related to rows and columns.

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to modify the method of Cima to use receptacles for placing agents, such as taught by Falsey, where the motivation would have been to use a powerful DNA microarray technology for arraying peptides and proteins to achieve rapid analysis of binding and functional properties of leads, as taught by Falsey, p. 346, right col. It would also have been obvious to one of ordinary skill in the art at the time of the instant invention to modify the method of Cima and Falsey to use statistical models for identifying agents producing a desired biological response, such as taught by Greco, where the motivation would have been to assess combination of agents that yield an unexpected enhanced pharmacological effect and the nature and intensity of drug interaction, as taught by Greco, p. 333, middle of right col; p. 334, top of right col.). Furthermore, it would have been obvious to one of ordinary skill in the art at the time of

the instant invention to use a Latin square design, as taught by A Field Guide, where the motivation would have been to control variations in two different directions, as taught by A Field Guide.

Applicants did not address the previous rejection in their response.

5. Claims 12-14 and 17-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cima, US 5,906,828, in view of Falsey, Bioconjugate Chem., 12:346-353 (2001), and further in view of Greco, Pharmacological *Rev.,* 47(2):33 1-385 (1995) and further in view of *A* Field Guide to Experimental Design, August 16,2000, at http://www.tfrec.wsu.edu/ANOVA/Latin.html, retrieved 5/30/2006 as applied to claims 1-3, 5-7, 11, and 19 above, and further in view of Chou, Advances in Enzyme Regulation, Vol. 22, p. 27-55 (1984). This rejection is modified from the previous Office action, but necessitated by amendment.

Cima, Falsey, Greco, and A Field Guide disclose a method of identifying agents capable of producing a desirable biological response, as set forth above. Greco also discloses repeating experiments for refining the design (p. 375, left col.).

Cima, Falsey, Greco and A Field Guide do not disclose concentrations of agents in receptacles.

Chou discloses quantitative analysis of dose-effect relationships in a mixture of agents for various biological systems from isolated proteins to intact animals (abstract). Chou discloses a number of examples analyzing the effect of multiple drugs and determining summation, synergism, and antagonism of drug combinations (p. 44,

Summary; example 1-5). Chou discloses using a constant molar ratio of two agents, a different total concentration of agent, and a different concentration of an agent (examples 1-5; fig. 2,4,6; tables 1-2).

It would also have been obvious to one of ordinary skill in the art at the time of the instant invention to modify the method of Cima, Falsey, and Greco to use varying concentrations of agents in a mixture, such as taught by Chou, where the motivation would have been to assess dose-dependent inhibition of cellular constituents by a combination of agents, as taught by Chou, abstract.

Applicants did not address the related rejection from the prior Office action in their response.

Conclusion

6. No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any

extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ritesh Agrawal whose telephone number is (571) 272-2906. The examiner can normally be reached on 8:30 AM - 5:00 PM M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Ritesh Agrawal RA

13 July 2007
JOHN S. BRUSCA, PH.D
PRIMARY EXAMINER